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BACKGROUND

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MEDICAL REHABILITATION: THE DOCTOR'S RESPONSIBILITY*

ALFRED R. SHANDS, JR., M. D.,
Wilmington, Del.

In the 18th century Cullen once wrote, "For when many new facts have been acquired, it becomes requisite that these should be incorporated into a system whereby not only particular subjects may be included, but the whole may be rendered more complete, consistent and useful."[9] This is the status of rehabilitation today. The war has been the means of acquiring an enormous volume of new facts on all types of subjects relating to the rehabilitation of the sick and wounded. Now it becomes requisite that this accumulation of new factual data be integrated into a system which will be "complete, consistent and useful" in the work of attaining the goal of rehabilitation, namely, "the restoration of the handicapped to the fullest physical, mental, social, vocational and economic usefulness of which they are capable."

Platt of England has appropriately divided rehabilitation into two stages, the first, medical, the second, social and industrial.[4] The purpose of this paper is to present to you some of the new data on medical rehabilitation. Based on this data, the author believes a new system of medical care is now evolving which will ultimately be incorporated into our present concepts of the practice of medicine and be as important a responsibility of the physician and his associates as prevention, diagnosis and treatment is today. This new system has been appropriately termed by Rusk "the third phase of medicine."

One of the great physicians of the 19th century was a Frenchman named Pierre Louis. He was the first to demonstrate and conclusively prove the value and importance of the use of statistics in the practice of medicine. Through his teachings, many accepted forms of therapy were proven to be in error and were discarded; many unaccepted forms were proven to be correct and were accepted. This was a revolutionary contribution to medicine in his day. A contemporary English physician of the great Louis once wrote in referring to his work, "Through medical statistics lies the most secure path to the philosophy of medicine."[9] The war has been the means of furnishing accurate statistics in many fields of medicine but in no field have these statistics been more important than in the field of rehabilitation. As a result many of the concepts of rehabilitation. have gone from the category of conjecture to one of exactitude. The path to our present day philosophy of the "third phase of medicine" is undoubtedly now being secured by these statistics.

First, what are some of the statistics on rehabilitation? During the war in our military hospitals there were two kinds of rehabilitation programs in this country planned primarily for two types of patients; one for the patient prior to combat or overseas duty, and the other for the patient subsequent to combat or overseas duty. The first program was administered almost entirely in the hospital and was largely medical rehabilitation. The second program was usually carried on in special convalescent centers and in addition to medical included social and industrial rehabilitation. A description of a typical case in the first program will give to the reader unfamiliar with the subject an idea of the operation of medical rehabilitation as practiced in the Armed Forces.[8]

Case Report: S/Sgt. Smith is a radio operator and a member of the crew of a Flying Fortress training at a Zone of Interior flying field. While on a routine training flight, Sgt. Smith's bomber had a crash landing and he suffered fractures of his back and right arm. After being taken to the hospital, his fractures were set and his back and arm placed in plaster casts. Following the accident his

* Read before the Medical Society of Delaware, Dover, October 8th, 1946.
** Medical Director, Alfred I. duPont Institute of the Nemours Foundation.

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first thought was: "How long a time will I be a patient?" On the fourth day after his admission to the hospital, he was interviewed by the Hospital Rehabilitation Officer. This officer obtained from Sgt. Smith's doctor the prescription for the quality and quantity of physical, mental and vocational activities he was to have while in the hospital, prescribed in the same way as medicines might be ordered. After this interview, he appreciated for the first time that the hospital staff was interested in him as the *individual* Sgt. Smith and not as a number in a hospital ward. He also realized the staff was more concerned with getting him out than keeping him in the hospital. This thought certainly did not disturb him as the crew of his bomber were "taking off" in 12 weeks for foreign duty and he did not want to be amongst the missing. So the question in his mind changed immediately from "How long a time will I be a patient?" to "How short a time can I be a patient?" He soon recognized the fact that the harder he worked on the prescribed program, not only the sooner would he return to his outfit, but also the better physical condition he would be in when he did. He was started immediately on physical reconditioning with bed exercises for his legs, good arm and shoulders. In a few days he was up walking and the amount of exercise was increased. He then went daily to the hospital radio shop, where he used not only his good hand but also the hand of the injured arm in a cast to work on radios; he increased his speed in sending and receiving with the telegraph key. He taught other soldier patients about radio operation and repair, and the Morse Code. With more time to concentrate on his military vocation, he rapidly became a more proficient radio operator. After the second or third week, he was going to the gymnasium of the Physical Therapy Department for special exercises and was participating in volley ball games. Lectures on subjects he had always been interested in were attended, entertaining and instructive selective reading became a part of his daily routine, and he found he had no spare time for activities other than those prescribed. By the end of each day he was both physically and mentally tired and there were no sleepless nights so often associated with a hospital. At the end of ten weeks his casts were off and after three weeks more he not only felt able to return, but was fully capable of going back to work. No refresher radio training was necessary. He joined his squadron immediately after being discharged, was able to to perform all of his full military duties and was in time to go overseas with his bomber crew. His discharge from the hospital was in 25 per cent less time than the average case with the same disabilities without rehabilitation, and Sgt. Smith well knew he was a better soldier mentally and physically than he had been when he entered the hospital three months before.

In the case of Sgt. Smith, military necessity was dictating a speedy rehabilitation and return to active duty in the minimum time. In many of the Army technical training schools in 1942-1943 instruction was given around the clock in 8-hour shifts. It was an absolute necessity for the Army to train the greatest number of men in the shortest possible time. This type of stimulus to rehabilitation during peacetime we know is non-existent, but with hospital beds at a premium and peacetime production demanding labor, we also know that there is still an urgent need to minimize hospital days and time lost from employment. Furthermore, how much better it is for the patient, his morale, and his economic status to be back on the job with the least possible delay.

Rehabilitation does not involve only the surgical patient for the medical patient is also involved. The tremendous value of rehabilitation to the medical case is exemplified in two A.A.F. medical service reports. One concerns a group of 645 virus pneumonia patients and the other pertains to a group of rheumatic fever patients.[7] Concerning the virus pneumonia patients, 50 per cent were given rehabilitation; 50 per cent were not. Those who received rehabilitation required 31 days of hospitalization, those who did not receive rehabilitation required 45 days, a difference of 14 days or 45 per cent more hospital time. There was a recurrence rate of 3 per cent amongst those with rehabilitation, 30 per cent amongst those without rehabilitation, 10 times as great. During 1943 and 1944, there were hundreds of soldiers with rheumatic fever in the A.A.F. hospitals in the Rocky Mountain area. Before a comprehensive re-

habilitation program, including graduated physical reconditioning, educational projects, etc., was instituted for these patients, 85 per cent of these were given a medical discharge. After rehabilitation was instituted, only 15 per cent were given a medical discharge. These two striking examples of what medical rehabilitation can do certainly show what an enormous saving of personnel and man-hours is involved. Rowntree has stated, "War is a great teacher. It will teach the individual doctor much and advance the science and art of medicine greatly, if we have but the vision and the will to learn."[6] Let us hope that we do have the wisdom and will to learn.

During the war a series of very exact experiments was performed by Ancel Keys in Minnesota on a group of conscientious objectors.[2] In the report of these experiments he uses the term "deconditioning" as contrasted to reconditioning. The deconditioning process is that of weakness, loss of strength and the accompanying changes which follow rest, particularly rest in bed. The subjects of the experiment were given complete bed rest for six weeks. The study showed in the whole group that there was a reduction in blood volume of from 10 to 20 per cent, an average reduction in the size of the heart of 11 per cent, an average decrease in reaction time of 5 per cent, a marked decrease in coordination, a disturbance in the vasomotor and proprioceptor adjustments, and a disturbance in the nitrogen and potassium balance. It was found that a normal nitrogen balance required double the amount of protein to be maintained. In addition, in many instances there was found to be constipation with occasional fecal impaction, postural hypotension, tachycardia, inability to void, especially in older men, and in some instances arthritic manifestations about the neck and shoulder girdle. With these conditions being produced in normal individuals, it certainly can be seen how in debilitating illness and disease in which ordinarily many of these changes are prone to occur, indiscriminate bed rest may enhance the deconditioning process and delay recovery.

With the findings of Ancel Keys in mind the question should be asked, "How can deconditioning best be avoided?" Hippocrates and Galen were some of our original teachers in this field of medicine. Hippocrates stated, "Exercise strengthens and inactivity wastes" while Galen wrote, "Employment is Nature's best physician." The basis for prevention of deconditioning is an active regime of exercise and employment, i.e. purposeful activity started at the earliest possible moment. The axioms of physical education are here most applicable for the prevention of deconditioning, namely, (1) exercise the whole body, (2) produce mild to moderate fatigue, not exhaustion, (3) provide some exercise every day, (4) adjust and graduate the program as rapidly as possible, (5) avoid sudden localized strain, and (6) make sure the patient is enjoying the reconditioning process. The natural voluntary efforts of the patient are often times more pleasing and effective than prescribed exercises. Sitting up in bed or in a wheelchair, periodic trips to the toilet, etc., are all useful either in prevention of deconditioning, or as a first stage of reconditioning. In most instances after illness, injury and surgery this type of activity can be commenced earlier than is the present practice in hospitals. As the convalescence progresses, more vigorous exercises are needed and an intensified program is called for. It should be pointed out that the exercises when given should be just to the point of fatigue. Certain forms of occupational therapy in which the patient can be interested may be most beneficial as a means of obtaining exercise for certain muscle groups. When the patient is ambulatory, the occupational therapy may be continued to great advantage in a hospital workshop, which was to be found during the war in nearly every military hospital. In a few instances, these shops in Army and Navy hospitals were elaborately equipped by industries who were interested in the rehabilitation of the soldier and sailor. These suggestions of exercise and employment will afford the patient an excellent means for minimizing or preventing a serious deconditioning process and aiding the physical reconditioning.

In exercising it should be remembered that every muscle fibre acts "as a sub-station" for the heart.[3] It is a minute pump and its pumping action enables the heart to carry its "enormous and relentless load" to every part of the body. It is not generally known, but it has

been definitely proven that the work of the heart is greater and the cardiac output is increased by changing from the sitting to the lying position. The amount of this increase is from 12 to 33 1/3 per cent; hence, the advantage of getting the patient in the sitting position as soon as possible is very evident, especially when the heart is involved. Dock states that the physician should treat bed rest with as much respect as morphine and digitalis[1] and undoubtedly in certain heart conditions, every day of recumbency increases the hazard to life.

The hazards of phlebothrombosis of the veins of the lower extremity and pelvis and pulmonary embolus are well known after surgery in older people, especially when prolonged recumbency is necessary. The extreme importance of early ambulation in this group after surgery has long been known and cannot be overemphasized. There have been many series of cases recently reported, showing the value of early mobilization after various types of surgery in all ages. Powers has reported 500 postoperative abdominal cases of all types,[5] some of these being operations as large and serious as gastric resections, and Whipple 1,000 similar cases,[10] in which the patients were out of bed on the first or second day after operation. The average hospital time for the 1500 cases was five days less than the hospital time for similar cases treated with bed rest and in Powers series the patients returned to work in four weeks less time. The postoperative complications were 50 per cent less. These statistics certainly afford convincing evidence of the value of early ambulation after surgery.

The statement has been made that the planned rehabilitation day with its disciplined program for the military patient cannot be transplanted in its entirety to civilian hospitals.[4] This is not wholly true. There is a great deal of the pattern of the sustained activity of the military hospital with its physical education, physical therapy, occupational therapy and educational and recreational projects which can be taken into the civilian institution to great advantage. The medical officers who were in the hospitals of the Armed Forces in this war and saw what was going on cannot help but realize the importance and value of this type of medical program to the practice of both military and civilian medicine. It is now our duty and responsibility as peace time physicians to take up where the war left off, establish systems both for the prevention of deconditioning as well as reconditioning and make medical rehabilitation programs worthwhile in our civilian hospitals.

There is no doubt that certain forms of medical practice go in cycles; what one generation may do, the next generation may condemn. This is well exemplified in the teachings of Benjamin Rush, called by some the Father of American Medicine. He taught that patients with all diseases should be purged and bled. In 1843, thirty years after his death, a famous physician stated that this teaching of Rush was, "Utter nonsense and unqualified absurdity." The analogy to rehabilitation is in the teaching of the great Weir Mitchell who in the last century wrote and preached total rest, for almost every disease and illness. Thousands were treated by bed rest and there is no doubt that thousands succumbed to degenerative disease and mental decay as a result.[3] Today we have such statements[3] appearing in the literature as, "Rest is a disease," or "Ease becomes often disease." "Ease softens us a trifle at first, prolonged it softens us much. In time ease makes us impotent in the face of hardship." If the medical lessons of this war and what has been demonstrated in many civilian hospitals during the last decade are to be fully appreciated and applied as they should, the hospitals of the future will not be filled with people lying in bed, but will be filled with people strenuously participating in programs of activity in order to get well and out of the hospital. Only the acutely ill will be allowed to rest. The doctrine of rest of Weir Mitchell will be as dead as the "bleed and purge" doctrine of Benjamin Rush was 30 years after his death. There has been a saying, "Better sitting than standing, better lying than sitting." This is a mistaken therapeutic idea. It has been now paraphrased to read, "Sooner dead, if lying; get up and get well."[2]

From the story of Sgt. Smith, the statistics of the A. A. F. virus pneumonia and rheumatic fever patients, the deconditioning experiments of Ancel Keys, the proven increased work load

on the heart in the lying position and the statistics of early mobilization after surgery, there is a lesson to be learned which we as doctors must not overlook. It is our responsibility to restore the sick and wounded to maximum usefulness in the minimum time. How better can this be done than by adding to our present systems of therapy a system of active medical rehabilitation so recently learned during World War II. This must be done, for it shall not be said that we as physicians are neglecting our duty in failing to apply to medical practice the concepts of the "third phase of medicine."

DISCUSSION

DR. I. M. FLINN, JR. (Wilmington): Dr. Shands has fairly well covered the field, I think. It is a philosophical subject as well as one that has tremendous practical values. During the war we came in contact with a considerable amount of this rehabilitation and, frankly, we hated it for the simple reason we were busy enough doing what we thought we should be doing. However, we had to follow through with it. There is no question about it. It is surprising how well the men did.

Now, just as an example, we had two or three of these hospitals in England, and there they developed, thanks to the British, some rehabilitation work. I never knew that a man could be trained to expand one side of his chest, but he can, and the remarkable thing about such treatment, in chest wounds and so forth, was the recovery following these exercises. It didn't take a man long to learn how to do it. It was most remarkable and the time in the hospital was cut down just that much thereby.

Another thing we used to do—it was sort of all on our own, but it was a good plan—if we had 45 or 46 knee cases in the hospital we put them all in beds right together. We would operate on them on the same day or within a day or two, and it wasn't long before you could go into the ward and see Tom looking over at Dick and saying, "What are you doing? How much motion have you got today?" And it was a race to get well. Nobody wanted to be behind the other one getting out of the hospital as quickly as he could. All of that comes under this same business of rehabilitation.

We also instituted at times—and I don't think this could be done in civilian life—rehabilitation of our whole ward. There were thirty beds in a ward, and we would get a tough old sergeant who happened to be lying there in bed and tell him he had to go ahead and start exercises for the whole outfit. Well, he would be there, and if some of them had something wrong with their arms and it was perfectly easy for them to raise their legs, he would have them lift their left leg and then their right leg and so on. The morale and everything else in that ward was much better, there was no question about it, but you had to have a tough sergeant.

One of the main contributions, I think, to the whole business of rehabilitation, and everything else that occurred in the European Theater, was the early mobilization of hands and feet.

We, being sort of back from the front, would receive patients in plaster casts with wounds in the hands, fractured bones, or compound wounds, it didn't matter much. Sometimes the cast would be left on in the hurry and bustle between four and five months, and there was a perfectly useless hand. You couldn't do anything for it.

So, Dr. Cleveland, who was then consultant in orthopedic surgery in the ETO, as he went around from hospital to hospital, said that no man regardless of injury, regardless of the position the bones were in, would be left in any sort of a splint more than three weeks, and it is remarkable the type of hands we got after that.

If we had one, for instance, where the index finger was involved, and the cast was on the whole hand for a period of two or three months, the whole hand was stiff and it took months of education and therapy to ever bring that hand back. If we left the cast on three weeks, the fellow could still use the fingers, and the time getting the man back to duty or getting him out of the hospital, or getting him out of the Army if the hand was bad enough, was cut down just that much.

All of these things come under rehabilitation. These are just a few practical examples, and I think that rehabilitation is certainly

coming into all the hospitals. I think it should, because there is no question in my mind that a patient who has gone through a course of training in rehabilitation is in much better physical shape when he gets through than the ones we are in the habit of treating.

DR. DAVID J. KING (Wilmington): This subject of rehabilitation, I think, is very interesting and highly instructive, and I believe it has been well presented and discussed. It always impressed me that the dogs in the experimental laboratory did so well after their surgery. No restraining or immobilization period was issued in the convalescent stages; nevertheless, they did very well. I remember looking at a dog's spine that had been operated on, Dr. Shands had done it sometime in the past, and I asked him how he kept his dog quiet after the operation and he said, "I didn't."

DR. GEORGE J. BOINES (Wilmington): I cannot resist the temptation, after hearing such a good description of rehabilitation by Dr. Shands, backed up by Dr. Flinn, to say a few words to bring to their attention what we have been doing in polio during the last four or five years while they have been in the Army. We have been doing exactly that. Medical rehabilitation, muscle training by people who were trained in muscle work, early mobilization and occupational therapy have all been done in Wilmington.

The result has been this: In 1941 when we were using the old methods of treatment our average hospitalization period was 160 days for all patients, paralytic and non-paralytic. In 1945 the hospitalization period was 32 days, and there was a much better improvement than in the patients we had in 1941 in spite of the long hospitalization period. I think this has been more or less of an emphasis in the newer method of rehabilitation and training of patients.

DR. N. W. VOSS (Wilmington): I would like to say that I certainly enjoyed these papers, but I want to also mention that these folks have been dealing with youth. It is very helpful indeed when you have dynamite to get an explosion and get action, but half of my patients are among the older people and the study of geriatrics is quite an interesting one. I frequently go over to the Home of the Merciful Rest and see some of those old ladies, and it is positively astonishing to me to see how they sit around and do a little knitting and almost nothing else and yet they live to be 90, and you seldom see them move an arm or leg or anything else.

You men have another proposition. Dr. Flinn, had the soldier boys who were the pick of the nation to work with. Dr. Shands has the children or youth of the nation, you might say, to deal with. We fellows have the old rheumatics, the arthritics and the fellows who say, "My God, Doctor, don't move that leg." and you have to inspire as well as treat, and believe me, you have a lot of inspiration to hand out sometimes. However, I certainly wish to compliment you men on your excellent papers, and it has been a treat to hear you.

DR. SHANDS: In conclusion I wish to thank the discussors for their interesting remarks on a subject which is becoming more and more important in medical practice.

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PARTIAL LOBECTOMY FOR BRONCHIECTASIS*

Case Report

G. A. BEATTY, M. D., and C. P. BAILEY, M. D., Wilmington, Del.

The occurrence of bronchiectasis following primary atypical pneumonia is apparently not well known, and little has been written on this subject. It is not mentioned as the cause of bronchiectasis in any articles on the subject, except that by E. B. Kay, who reports twenty such cases. Bronchiectasis is a chronic disease in which the symptoms are usually present for several years before a physician is consulted, at which time a history of repeated attacks of pneumonia or respira-

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tory infections is given, which the patient considers to be the cause of his symptoms. "It is rare for patients with bronchiectasis to be seen whose cough, sputum and general debility have been of only several months duration."[1]

Certain pathological factors are present in primary atypical pneumonia which are conducive to the formation of bronchiectasis. Kneeland and Smetana[2] reported one death in fifty-two cases. The microscopic appearance of the lungs showed occasional septa to be thickened by fibrous tissue and infiltrations consisting of mononuclear wandering cells and polymorphonuclear leukocytes. Some alveoli showed large mononuclear cells arranged in rows about the periphery. An occasional hyaline membrane was present. The mucosa of the larger bronchi and trachea was densely infiltrated by polymorphonuclear leukocytes and mononuclear wandering cells. The epithelial lining cells were prominent and frequently projected into the lumen which contained mucopurulent exudate and debris. In summary the alveoli, interstitium, and bronchi were the areas affected by this disease. The anatomic diagnosis was lobular pneumonia with organization and acute tracheo-bronchitis. Numerous other reports[3] show that it is noted clinically, roentgenologically, and pathologically that atypical pneumonia, in addition to interstitial pneumonitis, may present two factors commonly described in the pathogenesis of bronchiectasis, namely, bronchial and bronchiolar infection and bronchial and bronchiolar occlusion.

The incidence of bronchiectasis following primary atypical pneumonia undoubtedly is small, but no statistics on this complication are available.

CASE REPORT

Miss J. S., student nurse, age 19, was admitted to the medical service on January 16, 1946, complaining of a severe head cold, temperature of 100° F. a non-productive cough. She said she felt "grippy" with generalized aches and chilly sensations for less than 24 hours. Physical examination on admission was negative except for congested nasal mucosa, and a slightly infected throat. Ten months prior to admission, a routine x-ray of the chest was clear. There were no illnesses in the interim. Blood count on admission was R. B. C. 5,200,000; HB 98% (15.3 gm.); W. B. C. 7,500; polys seg. 57%; polys non-seg. 4%; lymphocytes 29%; monocytes, 8%; eosinophiles 1%; basophiles 1%; Sedimentation rate 15 mm. in one hour. Urinalysis was negative. Flat x-ray plate of chest revealed an area of infiltration at the right base extending from the dome of the diaphragm to the eighth posterior interspace. There was no involvement of the costo-phrenic angle. (Fig. I.) A lateral

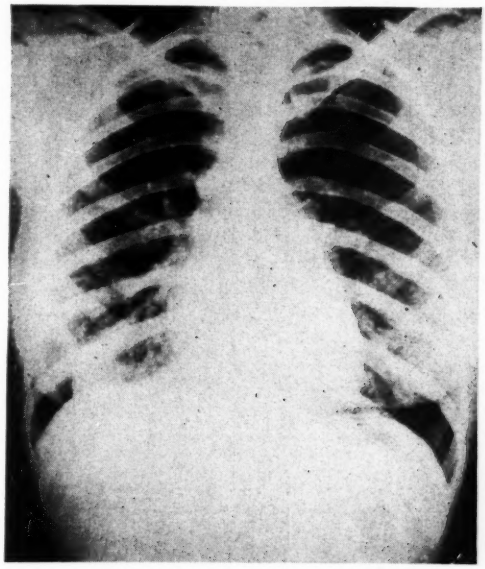

Fig. I. Flat plate showing infiltration at right base.

x-ray plate of the chest showed the area to be posterior against the chest wall. Three days later on January 20th, she showed abnormal physical signs for the first time when diminished breath sounds, and fine rales were heard at the right base posteriorly below the eighth rib. On January 20th, four days after admission, her cough became productive and her temperature was normal. She felt fairly well following this, and continued to run a normal temperature though her cough became slightly more productive and she felt weak and tired and had moderate sweats. She was discharged on January 24th, eight days after admission, to go home on convalescent leave.

Her cough gradually became more productive and on February 24th she was readmitted with a temperature of 100° F. Her sputum at this time measured about one ounce in 24

hours. The chest x-ray remained unchanged. She was discharged four days later. On October 14th the patient had a sudden hemoptysis of several ounces of bright red blood. She was hospitalized for bronchoscopy and bronchograms. Bronchoscopy was negative and the bronchograms on November 18, 1946, using lipiodol were reported as follows: "Bronchograms show normal filling of the bronchi in the left lung. The bronchi in the posterior portion of the right lower lobe shows a definite clustering and broadening throughout their entire length. This has the appearance of a cylindrical bronchiectasis. No saccules can be demonstrated. Bronchiectasis can be limited to the posterior portion of the right lower lobe." (Fig. II.)

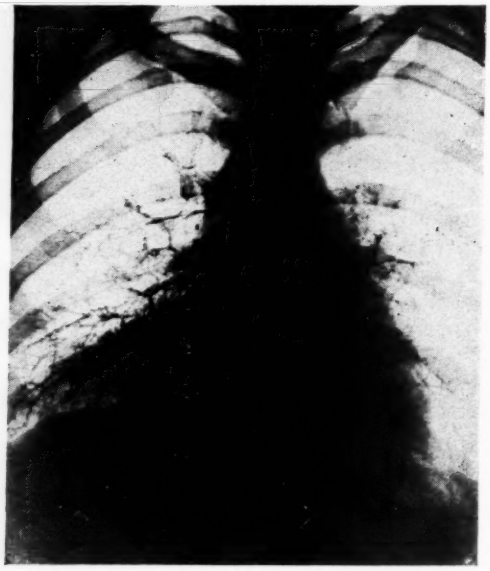

Fig. II. Bronchogram showing cylindrical bronchiectasis.

On November 21, 1946, the patient was operated upon by one of us (C. P. B.), who removed the posterior bronchial segment of the right lower lobe. Her recovery was uneventful, she was out of bed on the third post-operative day and discharged on the ninth post-operative day. She has remained well since.

Grossly the specimen of lung removed at operation measured 8x4x7 cm. Surrounding dilated bronchi there was an area of firm rubbery tissue measuring 5x2 cm. which was sharply demarcated from the surrounding normal tissue. At the periphery of the involved portion, what appeared to be bronchioles were dilated up to 2½ cm. and contained a green-yellow caseous material. Microscopic section of the lung revealed an extensive granulous reaction around small prominent bronchioles. There was extensive hyalinized fibrosis. Evident alveoli were collapsed and showed thickened walls. Throughout the granuloma there were frequent pseudo-tubercles containing amorphous acidophilic caseous centers and numerous foreign body multi-nucleated giant cells. (Fig. III.) A few of the more dilated aveoli were filled with large numbers of foamy, slightly refractile large lipocytes. Sudan IV fat stains revealed positive lipoid-staining material in the giant cells, tubercles, bronchial epithelium, and generally diffusely scattered throughout the fibrosing granulomatous portion. Acid fast stains were negative. Sections through the dilated bronchioles showed edema, epithelial hyperplasia, and surrounding round cell infiltration, typical of bronchiectasis. Diagnosis: bronchiectasis, with foreign body (lipoidal) granuloma.

Fig. III. Photomicrograph of Lung (x145) thru lipiodol granuloma showing pseudo-tubercles, foreign body giant cells, round cell infiltration and dilated bronchioles.

COMMENT

The use of iodized oil in bronchograms for diagnostic purposes is not uncommon; it has generally been assumed to produce no local reaction and to be readily disposed of by the body. Numerous animal experiments[4] are recorded indicating that the use of iodized oils are innocuous. A few cases of tissue reaction to iodized oil are reported.[4,5] Some observers have suggested that such a tissue reaction is "the normal walling off of a foreign body that cannot be removed rather than a reaction attributable to the chemical nature of the oil."[6]

Dr. R. P. Custer[7] commenting on the lungs studied during the war at the Army Medical School Institute of Pathology reports that granulomatous changes following lipoidol were not uncommon in their series. In this case there is marked tissue change present one month after the installation of the oil. These findings suggest that, while the installation of iodized oil may be without reaction and eventually removed in normal lungs, in those showing pathology a granulomatous reaction may occur.

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STREPTOMYCIN IN TYPHOID FEVER*
Report of a Treatment Failure

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The status of streptomycin in the treatment of typhoid fever has not been completely established at this date. The questions of fatality rate reduction, favorable influence on complications, maximum drug dosage, and acquired *in vivo* resistance remain to be fully answered. Although apparently a treatment failure, this case is presented to illustrate the ramifications of such an infection, its treatment with an antibiotic, and the problems that arise therefrom.

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CASE REPORT

The patient, a twenty-four-year-old Negress, was admitted to this hospital on July 16, 1946, with a chief complaint of chills and fever. The onset of illness occurred five weeks prior to admission, and was initiated by severe shaking chills which were irregular in occurrence and duration. At that time a diagnosis of upper respiratory infection was made, and temporary improvement was noted under symptomatic therapy. After several days, however, hemoptysis and night sweats occurred. These findings, along with a previous history suggesting pulmonary pathology, warranted hospital admission for further study.

On admission, a young, emaciated, delirious and acutely ill, colored female was observed, with a temperature of 106° F., pulse rate of 105, and an essentially normal physical examination. Admission laboratory studies showed:

> RBC, 4.1 million; Hemoglobin, 10.6 gm.; WBC, 7,700 with a marked left shift. Urinalysis showed a specific gravity of 1.021, a 2 plus albumin, and a normal microscopic. Serology, negative on blood and spinal fluid. Febrile agglutinins were negative, except for a positive titer of 1:20 against typhoid O, and a 1:80 titer against typhoid H antigens (these increased to titers of 1:160, 6 days later), and negative sputum and cerebrospinal fluid findings.

Two x-ray films of the chest showed no pathology.

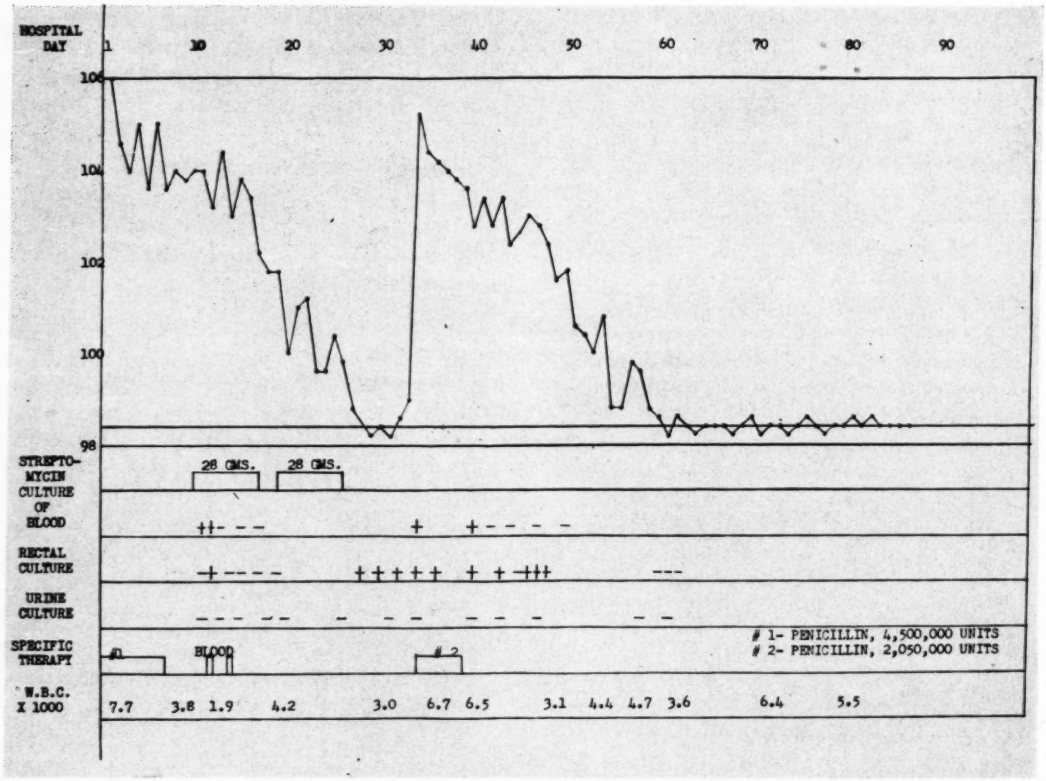
Eberthella typhosa was isolated from blood, urine and rectal cultures made on the 5th and 8th hospital days. This strain showed a sensitivity to streptomycin of 10 meg. per ml., using a two-fold tube dilution in modified nutrient broth,[1] controlled with a standard reference strain of *B. circulans* (regularly inhibited by 0.3 meg. of streptomycin). These cultural findings confirmed the clinical impression of typhoid fever, suggested by a later statement of the family that the patient suffered 8 to 10 foul-smelling, watery stools daily, two weeks before admission.

Having fulfilled the bacteriological and sensitivity requirements for a clinical trial of streptomycin therapy, 28 gm. of the hydro-

chloride* was promptly obtained through the courtesy of Dr. Chester S. Keefer**, who recommended that it be given in 4 gm. daily dose, by intermittent intramuscular injection. Starting on the 8th hospital day, 0.5 gm. of the drug is 5 ml. of isotonic sodium chloride solution was administered every three hours, for 7 days. During this time the temperature fell and cultures became negative; but the patient suffered a severe hemorrhage from the bowel, with a fall in RBC to 1.8 million. Two 500 ml. whole blood transfusions were administered, and the patient responded satisfactorily, with no further bowel complications.

Due to a misunderstanding, there was a delay in obtaining the second 28 gm. course of streptomycin, the patient being without the drug for 2 days. Following the administration of this lot (given as previously described), there was no alteration in a rather favorable course. The temperature became normal one day after completion of this course (27th hospital day), and remained normal for one week. Streptomycin blood levels[1] averaged 80 meg. per ml. of serum (40-320 meg./ml.) during both courses of therapy.

On her 33rd hospital day the patient suffered a severe relapse, with abrupt rise of temperature (see chart), and a return of positive blood and rectal cultures. The *Eberthella typhosa* isolated from these cultures showed a streptomycin sensitivity of 300 meg. per ml., a *thirtyfold increase in resistance* over the original isolation. Two million units of penicillin were administered intramuscularly, along with symptomatic therapy. During a prolonged convalescence of 50 days, the temperature became normal by lysis, and the patient was discharged in an improved condition October 10, 1946, 90 days after admission.



DISCUSSION

From the accumulated evidence in the treatment of 51 cases of typhoid fever with streptomycin, Keefer et al[2] concluded that the

* Supplied through the kindness of Merck and Co., Rahway, N. J.

** Chairman, Committee on Chemotherapeutics and Other Agents, National Research Council.

results were disappointing. The majority of patients received 4 grams of the drug parenterally for about 7 days, and when given after the 18th day of illness, normal temperatures occurred only after the 28th day. Combined oral and parenteral therapy was apparently no better than parenteral therapy alone. The question of whether the drug if given in the first 7 days, would shorten the duration, was raised. No increased *in vitro* resistance studies were reported.

The problems of the treatment of a deep-seated infection with streptomycin have been considered in many recent reports. Reiman et al[3] were the first to point out that if typhoid bacilli reside and multiply in plasma cells and macrophages, they may not be affected by streptomycin unless they escape into the blood and tissues. Bondi et al[4] noted that streptomycin activity was markedly reduced under *in vitro* anaerobic conditions, and suggested that in parts of the body where a reduced oxygen tension existed, as in the feces, greatly increased concentrations of the antibiotic may be necessary to inhibit growth. Welch et al[5] reported that streptomycin in minimal dosage exerted a growth-stimulating effect and an increased fatality rate in white mice injected intraperitoneally with *E. typhosa*.

From a series of carefully controlled experiments Klein and Kimmelman[6] concluded that the *in vitro* development of streptomycin resistance in 12 strains of shigellae was the result of spontaneously occurring resistant variants, which selectively developed in high concentrations of streptomycin. These authors suggested that in a culture isolated from a clinical infection, a large number of susceptible cells may occur along with a few resistant variants, the latter not being detected by the conventional methods of susceptibility testing (wherein relatively small inoculums are used). When streptomycin therapy is instituted, the susceptible bacteria are rapidly eliminated. If the body defenses do not destroy the resistant forms, these then may multiply to a point where even maximum drug concentrations would not eliminate them.

Such a condition is well illustrated in a clinical report recently presented by Bondi et al.[7] Two cases of urinary tract infections were unsuccessfully treated by streptomycin, due to the development of a resistant variant. These authors demonstrated the presence of this variant in the *original parent culture* (sensitivity 1 meg.) by testing the susceptibility of a large population (5 billion cells) of this culture and noting the development of 2 colonies not inhibited by 1000 meg. of streptomycin. These variants appeared to remain permanently resistant, both *in vitro* and *in vivo*.

These observations, along with the fact that *in vivo* streptomycin resistance can occur extremely rapidly (24 hours), may serve to explain the treatment failure in the case presented. It appears probable that if streptomycin reached the intestinal walls in less-than-bactericidal concentration during the first course of treatment, the 2 day lapse before the second course was started may have permitted the development of a resistant variant, the multiplication of which initiated the subsequent clinical relapse.

CONCLUSIONS

A case of typhoid fever treated with 56 gm. of streptomycin, has been presented. The drug was given in two courses of 28 gm. (each course 4 gm. a day for 7 days), administered by the intermittent intramuscular route. There was in interval of 2 days between courses when no drug was given. The *E. typhosa* first isolated from blood cultures was inhibited *in vitro* by 10 micograms of streptomycin, a subsequent isolate after completion of therapy requiring 300 micrograms for inhibition. Adequate blood serum levels were attained. No evidence of local reaction, histamine-like effects, sensitization or neurological disturbances was noted. The patient suffered a clinical typhoid relapse, with a recurrence of positive blood cultures 9 days after streptomycin had been discontinued, and made a slow but uneventful convalescence. The mechanism of increased streptomycin resistance was discussed. It is concluded from the case presented that streptomycin exerted at best only a palliative effect, and its place in the treatment of typhoid fever has yet to be established.

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EOSINOPHILIC LEUKEMIA*
Case Report**

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Eosinophilic leukemia is a rare disorder. Most of the papers dealing with the disease are merely case reports since no one author has collected enough material to satisfactorily analyze the disease. However, in review of the cases reported up to 1938 Forkner[1] lists six cases of acute eosinophilic leukemia and about a dozen collected cases of chronic eosinophilic leukemia. In the reported cases the counts vary greatly in numbers of leukocytes per cmm., the lowest being 6,900 and the highest 236,000 cells per cmm.

This case is presented as an example of the difficulty of making the diagnosis of eosinophilic leukemia in the absence of a very high white count.

Obviously the blood count on an individual with eosinophilic leukemia will show a marked increase in the numbers of eosinophiles. However, in those individuals with a white blood count which is not remarkably elevated a problem of differential diagnosis arises. In many parasite disorders eosinophilia may be as high as 70%, particularly in trichinosis. In normal individuals 10-25% eosinophilia has been demonstrated with no other abnormalities noted and no disease extant. Therefore, eosinophilia itself may not mean disease. Allergic disorders rarely may cause a high eosinophilia and it has been observed that the bite of the black widow spider causes marked eosinophilia. In cases of periarteritis nodosa the eosinophilia is frequently as high as 70% and in occasional instances the total white count may be as high as 50,000 cells per cmm. Patients receiving liver therapy for pernicious anemia show an increase in the eosinophile count in about 30% of the cases.[2]

CASE REPORT

The patient, G. H., a 55-year-old white married male truck driver, first entered the Delaware Hospital in September, 1945, complaining of weakness and a productive cough of eight months' duration. Initial studies revealed a moderately severe macrocytic, hyperchromic anemia, and a leucocytic count of 19,000 with 72% eosinophiles. The eosinophilia persisted, the leucocytes ranging between 5,400 and 39,000 and the eosinophilia between 40-82%. (Fig. I). Repeated studies,

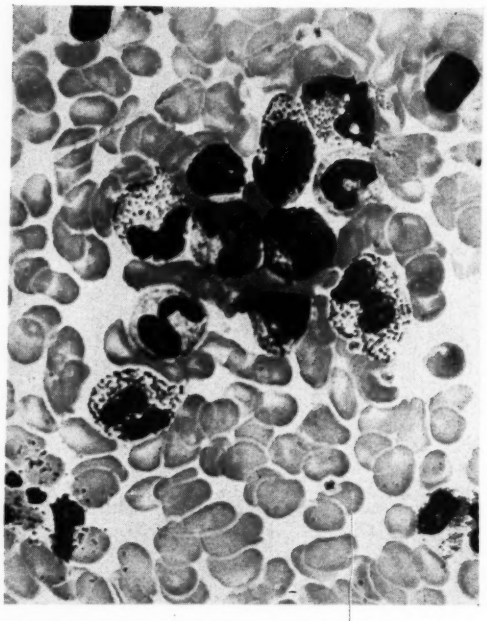

Fig. 1. Peripheral blood smear (x945) showing marked increase in number of eosinophiles.

which included blood and sputum cultures, repeated stool examinations for ova and parasites, and skin tests for trichinosis— all were within normal limits. Microscopic examination of the sternal bone marrow, obtained by sternal puncture, revealed appreciable increase in adult eosinophilia corresponding in maturity to those seen in peripheral blood. There appeared to be no tendency to leukemia hyperplasia, but there was a surprising deficiency of young red cells.

Blood complement fixation studies at the U. S. Public Health Service Laboratory at Bethesda, Maryland, revealed negative reactions for trichinosis and amebiasis, but a positive complement fixation for echinococcus disease. At that time the Public Health Service cautioned that the test might be unreliable due to the age of the antigen. The patient improved on symptomatic treatment, and was discharged on November 6, 1945.

During the ensuing eight months, under the

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** From the services of Dr. B. B. G. Blackstone, Dr. M. F. Squires and Dr. J. M. Messick.

care of his physician, he received eighteen blood transfusions because of increasingly severe anemia. The high eosinophilia continued. Because the patient became discouraged at "living on other people's blood," he ran the usual gamut, finally resorting to "manipulators" in an effort to cure his weakness and restore his blood to normal.

In May, 1946, he was readmitted to the hospital with a provisional diagnosis of echinococcus disease. Additional multiple, vague complaints included frontal headache, "crick" in the neck, which was aggravated by motion, and soreness in the region of the right sternocleidomastoid muscle, which was not constant, but which radiated to the right shoulder. The cough now occurred chiefly after being in the recumbent position for a few hours, and was productive of a frothy sputum. There was no history of allergy. He had noted slight edema of the ankles, but not of the face. He complained of gnawing abdominal pains which occurred without periodicity and were not influenced by eating. Borborygmus and meteorism were constant complaints. There had been a total weight loss of 30 pounds. Finally, he complained of impotence which began with the onset of his illness.

The patient had resided in Delaware, except for a two weeks' vacation, and a few motor trips to Florida. He had had no contact with animals other than his own dog and cat, both of which has been obtained after the onset of symptoms.

Physical examination revealed a pale, lethargic and extremely discouraged white male, apparently in his sixth decade, who was in no acute distress. The positive physical findings included some limitation of motion in lateral rotation of the head with an audible "clicking" sound in the neck, slight tenderness over the frontal areas, a slight post-nasal discharge, and poor oral hygiene with several loose, carious teeth. The liver was palpable 4 cm. below the costal margin in the midsternal line. The surface was smooth, and the edge was sharp. The spleen was palpable 5 cm. below the left costal margin. There was moderate atrophy of the muscles of the right upper arm, the difference in circumference between the right and left sides being 2½ cm. The remainder of the physical and neurologic examinations were negative.

Laboratory studies showed: Hemoglobin 10 gm. (64%); R. B. C. 2,900,000; W. B. C. 18,200; polys 19%, of which 2% were nonsegmented; lymphocytes 17%; basophiles 1%; eosinophiles 63%. Repeated urinalyses were negative, including a spectrographic test for porphyrin. Numerous examinations of the stools failed to reveal the presence of ova, parasites, or cocult blood. Sputum and nasal smears were negative for eosinophils. Gastric content contained free hydrochloric acid. The sedimentation rate was 27 mm. in 60 minutes using Cutler tubes. Blood serology was negative. The blood type was Type A, Rh positive. Roentgenologic examination of the entire gastro-intestinal tract was negative; examination of the cervical spine revealed an old fracture of the fifth cervical vertebra.

Pathological examination of a biopsy taken from the right biceps muscle revealed no evidence of parasites or of any vascular abnormalities in more than 100 sections studied.

Because studies had failed to reveal a definite etiologic basis for the eosinophilia, and because the provisional diagnosis of the echinococcus disease as suggested by the positive complement fixation test had not been confirmed, it was decided to investigate the liver roentgenographically to exclude, if possible, the presence of cysts of this organ. Accordingly, a hepatogram was made with the aid of thorotrast. Following the technique of Yeater, et al,[3] the thorotrast was injected intravenously every 24 hours in three consecutive days, and the roentgenogram was made on the fourth day. The visualization of the liver and spleen were entirely normal and there was no evidence of cysts. (Fig. II). The patient had no ill effects from this study.

A sternal biopsy was performed and microscopic examination of the sternal marrow revealed hyperplasia consisting almost entirely of eosinophils, the majority of which were mature. There were numerous young eosinophils. In the adult forms the eosinophilic granules were spotty and frequently sparse in number, similar to those in the peripheral smear. The marrow showed marked depletion of the erythropoietic elements, and there were few neutrophiles. Megakaryocytes were common.

A diagnosis of chronic eosinophilic myelogenous leukemia was made and the slides and

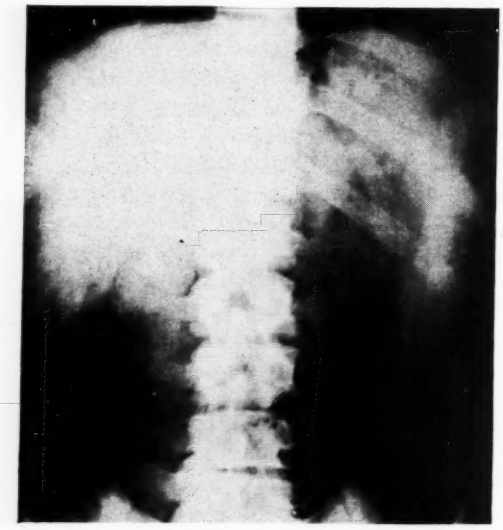

Fig. II. Thorotrast visualization of liver and spleen showing no abnormalities.

clinical history were reviewed by Dr. R. P. Custer who concurred with the diagnosis.

From the beginning the diagnosis of eosinophilic leukemia was considered, but because of

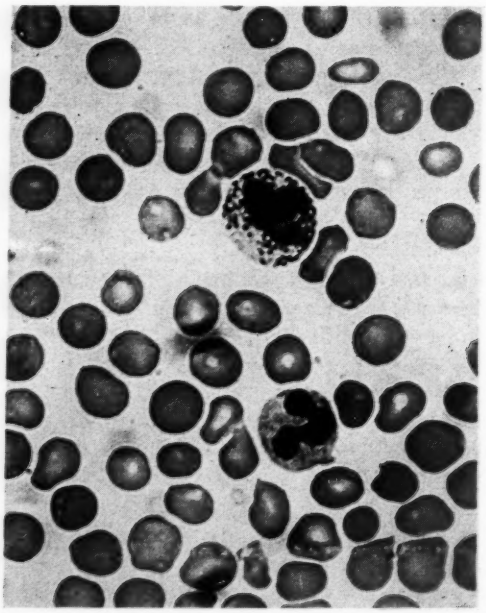

Fig. III. Peripheral blood (x850) showing sparsity of eosinophilic granules.

the rarity of the disease and numerous other causes of eosinophilia all other possibilities were ruled out before the diagnosis was made. In the study of this patient every effort was made to determine a cause of eosinophilia other than eosinophilic leukemia. All efforts were unsuccessful.

The finding of a few scattered eosinophilic granules in the cytoplasm of the eosinophile, instead of the hundreds usually seen, is reported as being typically diagnostic of eosinophilic leukemia.[4] These findings were noted in this case in the peripheral blood (Fig. III) and in the bone marrow. On the basis of the clinical history, marked anemia, atypical eosinophiles in the blood and bone marrow, and the inability to find any other cause for the eosinophilia a diagnosis of eosinophilic leukemia was made.

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DIAPHRAGMATIC EVENTRATION*

Case Report

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Eventration of the diaphragm is a condition in which one of the domes of the diaphragm is in the form of a thin fibrous sheath ballooned up into the thorax by the pressure of the abdominal viscera on the affected side. The effect of the displacement of viscera to the thoracic level may produce symptoms of a severity to require medical attention. The following case is presented to demonstrate the diagnostic radiological findings and the symptoms of a marked left diaphragmatic eventration.

J. O., a twenty-three-year-old white male, complained to his doctor that for the last year he has had a pulling sensation through the upper abdomen. This was also associated with slight pain and passing of gas about 1½ to 3 hours after a heavy meal. Bending forward or doubling up seemed to relieve his distress.

He gave a history of having been perfectly well until the age of seventeen when he was

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injured in an automobile accident. Although he had severe left shoulder and chest contusions, there was no x-ray evidence of fracture. However, he coughed small amounts of bright blood immediately after the injury and had severe pain through the upper left chest, shoulder, and neck. This persisted along with neck

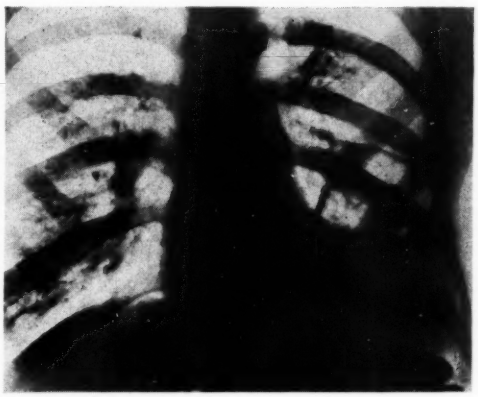

Fig. I. Film taken in the upright position shows barium entering the cardia at the normal level and passing upward through the inverted stomach.

stiffness for several months. He was able to return to work and felt well until the present symptoms began one year ago. He has been doing industrial painting for the past one and one-half years. Three years ago he was told he had a high left diaphragm after a check-up chest film for merchant marine service.

Fluoroscopic examination at the present time showed a normal right chest and diaphragm. The dome of the left diaphragm was elevated to the level of the fourth anterior interspace and contained gas from both the stomach and large bowel. The thin diaphragm showed no movement with respiration.

Barium passed through the esophagus without delay and entered the stomach at the normal level. There appeared to be a complete reversal of the position of the stomach, the cardia pointing downward and the body upward, extending into the dome. The pylorus was then seen to be directed downward toward the fundus. All of the stomach as well as the duodenal cap filled well fluoroscopically. A twenty-four-hour film showed the head of the meal in the descending colon. Particles of barium were seen to extend above the normal level of the diaphragm in the gas distended splenic flexure. After it was determined that there was no movement of the high left diaphragm, a diagnosis of eventration was made.

The radiographs show the anatomic relationships and distortion described: (Figs. I, II, III).

Fig. II. Film taken in the Trendelenberg position shows the extreme rotation of the stomach.

Fig. III. Eventration of the left diaphragm. Notice the high position of the stomach bubble and flecks of barium in the splenic flexure, contained under the intact diaphragm.

ETIOLOGY

The condition is described as being the result either of congenital defects or of a disturbance of the phrenic nerve supply. The roentgenologic appearance is similar in any case. Since phrenicectomy has been a recognized form of treatment in pulmonary tuberculosis and other pulmonary illnesses, eventration from this cause is most frequently seen at the present time. A certain number of cases of eventration also are the result of phrenic nerve paralysis acquired by wounds in the neck or by pressure in the neck or thorax, especially mediastinal tumors.

In the absence of a history of phrenic nerve injury, the etiology is obscure but is attributed to idiopathic or congenital defects. Whether the primary defect is in lung development with a secondary elevation of the diaphragm or whether the diaphragmatic relaxation is primary, has not been shown. Since most congenital diaphragmatic eventrations are left sided, it is possible that chronic overdistension of the stomach and colon may be a factor in stretching the congenitally weak diaphragmatic musculature. The solid liver mass on the right protects this side from tension.

PATHOLOGY

The dome of the relaxed diaphragm is displaced upward two to three interspaces, usually to about the level of the fourth interspace anteriorly. It consists of a serosal-covered, thin, fibrous sheath in which the musculature is atrophic or almost absent.

SYMPTOMS

Usually diaphragmatic eventration produces no symptoms. When present, they are referable to disturbances in gastro-intestinal function and in some cases to pulmonary and cardiac embarrassment.

Pain, which is the most common symptom, is variously described as a tugging, burning, bloating or sensation of a mass in the epigastrium. The pain may be referred to the back, upper thorax, left shoulder or arm, and may be initiated or aggravated by eating, strenuous work and exercise.

RADIOLOGICAL FINDINGS

The diagnosis of diaphragmatic eventration is made from x-ray findings and is to be differentiated from diaphragmatic hernia.

The outline of the diaphragm on the left is high and bowlike with the air filled fundus and splenic flexure beneath. The dome forms a smooth arc, occasionally this is interrupted by a small notch which is located at the superior point of apposition between the colon and fundus. The dome on the right side is not elevated and shows no gas beneath.

The demonstration of a high diaphragm that shows paradoxical movements or no excursion at all is of prime importance in the differentiation from hernia of the diaphragm. Thus, careful fluoroscopic observation and adequate films in all positions are necessary. The movements, sometimes absent, are more commonly paradoxical, exhibiting an upward excursion on inspiration, and vice versa. With herniation, if any part of the diaphragm is visible, it exhibits a normal respiratory excursion.

Gastric deformity is an additional x-ray finding which is fairly constant. There are various degrees of upward displacement of the greater curve of the stomach which rotates on its fixed points at the cardia and pylorus. The fundus and pylorus as a result of the torsion, may become the lowest portions of the stomach, as demonstrated on these radiographs.

When a barium meal is given, the opaque medium is seen to enter the fundus at a low level and travel upward and over the lesser curvature at an acute angle to the pylorus, which usually lies close to the fundus. The resulting bilocular appearance may amount almost to that of a volvulus. A film taken twenty-four hours after the ingestion of the meal may show barium at the thoracic level in the splenic flexure of the colon.

Lung tissue is visible through the dome of the diaphragm if the gaseous distension of the stomach is considerable and the lung posteriorly is normally expanded.

The contour of the diaphragm, its position, and the nature of its movements present the most constant and diagnostic signs of eventration.

Palliative measures are usually unsuccessful in the treatment of diaphragmatic eventration. Surgical repair is also unsatisfactory.

SUBACUTE BACTERIAL ENDOCARDITIS DUE TO AN H. INFLUENZAE - LIKE ORGANISM*

Case Report

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The use of streptomycin in certain cases of bacteremia due to Gram-negative bacilli seems well established, since evidence shows that the drug not only exerts a favorable effect in clearing the blood stream of organisms, but also influences favorably any local infection at its site. Keefer et. al.,[1] reporting on streptomycin in infections, include eight cases of bacteremia in which the infecting organism was *H. influenzae*. All of these patients improved or recovered.[2]

Alexander and Leidy,[3] working with type b *H. influenzae*, suggest a high degree of sensitivity of this organism to streptomycin. Experiments indicate that the protective power of streptomycin for mice against this organism is equal if not superior to the combined use of sulfadiazine and specific serum or sulfadiazine alone. The use of streptomycin therapeutically apparently avoids the danger of toxicity associated with the prolonged administration of sulfonamides.

Logan and Herrell,[4] in commenting on the use of streptomycin in *H. influenzae* meningitis in children, corroborate the efficacy of the drug; particularly the clinical and laboratory improvement following its use after the apparent failure of sulfadiazine and serum therapy. A certain parallel may be seen in the case presented here.

The following case is reported as one of septicemia due to an atypical *H. influenzae* superimposed on a long-standing mitral insufficiency of probable rheumatic origin.

The case is significant in: (1) the absence of an obvious primary site of infection, and (2) the response to streptomycin therapy suggesting prompt sterilization of the blood stream after an active course of six weeks' duration. Streptomycin was administered, after a short preliminary trial of sulfadiazine, in order to avoid an incipient sulfonamide toxicity, as evidenced by renal irritation and a decline in the hemoglobin and red blood cell count.

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CASE REPORT

M. F. D., male, white, age 59, was admitted to the Medical Service of the Delaware Hospital on September 3, 1946, complaining of daily chills and fever of six weeks' duration, occurring after prolonged exposure to sun while fishing. Following this onset the patient had been admitted to another hospital, where numerous blood smears were reported negative for malarial parasites, and a vigorous but ineffective course of penicillin therapy was carried out. Twenty-four hours before the present admission he developed a sudden and severe pain in the left upper quadrant and flank which lasted 8 to 12 hours. He vomited once on the day of admission and reported a weight loss of 15 to 17 pounds during his illness. The past history significantly revealed scarlet fever during adolescence in France, complicated by a known "heart murmur." This murmur had persisted, and, at the age of 21 years, x-ray reported an "enlarged heart." In 1941 he had been hospitalized for "gall bladder colic."

Physical examination on admission showed a temperature of 98.6 F., pulse rate 120 and respirations 28. He appeared acutely but not critically ill. The skin over the lower extremities showed several small superficial areas suggesting petechiae. The buccal mucosa showed scattered patches of a whitish, mucoid exudate. The posterior nasopharynx was slightly injected. There was no regional or general glandular enlargement. The chest was symmetrical and expanded equally; the lung fields were clear to percussion and auscultation. The cardiac rhythm was regular. The apical impulse was in the fifth interspace in the mid-clavicular line. There was a grade III systolic murmur at the cardiac apex and to the left of the sternum. The abdomen was resistant to palpation and diffusely tender in both upper quadrants. Neurological examination was not remarkable; there was no meningismus.

Laboratory studies revealed R. B. C. 4.3 million; Hb. 12.3 gms. (78%); W. B. C. 16,700; segmented polys 84%; non-segmented polys 7%; lymphocytes 5%; monocytes 2%; eosinophiles and basophiles each 1%. Subse-

quent blood counts showed a persistent decrease in the hemoglobin and red blood cell counts to 7.9 gms. (50%) and 2.9 million, respectively. Urinalysis was essentially negative except for one plus albumin. The blood urea nitrogen was 19.0 mgms. % and the fasting blood sugar 108 mgms. %. On September 6, a scanty growth of E. coli and an enterococcus occurred in culture of the urine. Scrapings from the petechial lesions showed no growth after 3 days' incubation. Routine febrile agglutinations including typhoid, paratyphoid, brucella, tularense, and proteus antigens were negative in all dilutions. The erythrocyte sedimentation rate was 26 mm. in 60 minutes. Chest x-ray showed the cardiac outline within upper normal limits but some increase in the vascular markings of both hilar trunks.

Bacteriological studies of the organism isolated on September 4, 1946, carried out by Mr. E. G. Scott, bacteriologist, Delaware Hospital, revealed a small, filamentous gram-negative rod first isolated from blood culture, and on 3 subsequent cultures. The organism grew as a non-hemolytic, convex colony 1-2 mm. in diameter, with an entire margin. Growth occurred slowly (2-4 days) but most abundantly on tryptose agar with 5% human blood, in 10% CO_2 at 37° C., and less readily on chocolatized proteose-peptone agar and fluid thioglycollate medium. No growth occurred on any of the above solid media incubated anaerobically, or at room temperature. Nu-

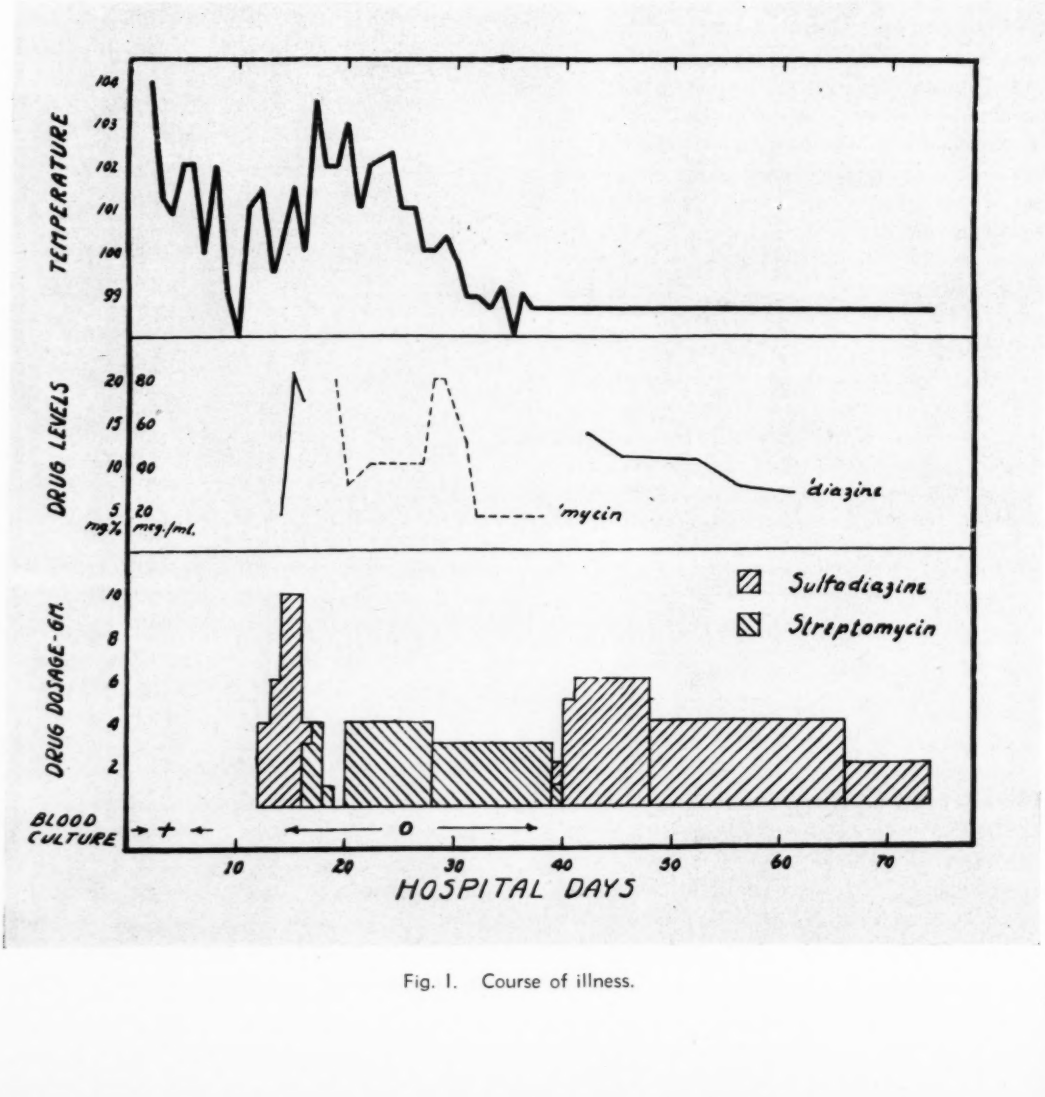

Fig. 1. Course of illness.

trient agar or tryptose broth did not support growth under any conditions. On a semisolid tryptose agar with ascitic fluid, the organism was non-motile, and promptly fermented dextrose, maltose, saccharose and lactose with the production of acid but no gas.

Agglutinations with anti-Brucella and anti-P. tularense sera were negative, and repeated attempts to demonstrate capsular swelling with anti-H. influenzae type b serum were negative, with a suggestion of a capsule in some preparations. The organism was finally considered to be an atypical member of the *H. influenzae* group.

In vitro studies with increasing concentrations of streptomycin showed the organism to be very sensitive to this antibiotic, being inhibited by 5 micrograms per ml., and growing in 1 microgram per ml.

On the day following admission the temperature spiked to 104 F. following a spontaneous chill. The temperature continued in a hectic course ranging from normal to 102 F. for eleven days, at which time intravenous and oral sulfadiazine were given to a maximal blood level of 20.3 mgms. % in 72 hours. On September 18, fourteen days after admission, sulfadiazine was discontinued and streptomycin therapy was begun in dosage of 4 gms. daily, 0.5 gms. q. 3 hours, by intramuscular injection. This dosage was continued and a daily blood level (taken at the end of the 3rd hour) of 40 micrograms per ml. serum (technic of Food and Drug Administration using B. circulans) was maintained for fifteen days, until October 1, except for a period of thirty-six hours 3 days after instituting therapy, when a progressive rise of temperature over a period of 48 hours suggested a toxic reaction to the drug. On resumption of therapy the temperature regressed gradually over eleven days, at which time streptomycin dosage was reduced to 2.4 gms. daily with average daily blood levels (taken at the end of the 3rd hour) of 15 micrograms per ml. serum until October 11, when the drug was discontinued and oral sulfadiazine resumed. Sulfadiazine blood levels of 13.0-15.0 mgms. % were maintained for two weeks and then discontinued after a period of slow withdrawal. Twenty blood cultures during and after cessation of therapy were negative for the infecting organism.

Supplementary therapy consisted of: parenteral fluids to maintain adequate water balance; two transfusions of whole citrated blood, each 500 cc., to combat an anemia of a hypochromic microcytic type apparently following intensive sulfonamide therapy; ascorbic acid 300 mgms. daily; and, when tolerated, a high caloric diet containing 125 gms. protein.

During the acute phase of his illness the patient developed sudden, transient and acute recurrences of left upper quadrant pain interpreted as multiple splenic or renal infarctions. These episodes could not be correlated with the periodic hematuria evidenced by frequent urinalyses. Local pain at the site of streptomycin injections was not alleviated by the addition of 0.75 ml. of 1% procaine to each dose. The streptomycin blood level, however, was apparently not affected by the use of the procaine. Throughout the period of observation there was no change in the character of the apical systolic cardiac murmur. An electrocardiogram taken on October 29, was essentially normal except for unusually large T waves in the precordial leads.

After hospitalization of 42 days the patient was discharged to continue convalescence at home under the care of his private physician. A blood culture on December 17, 1946, showed no growth after 10 days' incubation. The patient's subsequent course is reported satisfactory.

SUMMARY

1. A case of subacute bacterial endocarditis due to *H. influenzae*-like organism successfully treated with streptomycin and sulfadiazine is reported.
2. The organism was sensitive *in vitro* to streptomycin.
3. Although the patient developed an apparent toxic reaction to heavy sulfonamide administration during the early therapeutic course, sulfadiazine was given later as supplemental therapy without untoward effect. It is presumed that the earlier findings were related to the blood stream infection rather than sulfonamide toxicity.

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+ Editorial +

The Year Ahead

The year 1947 bids fair to be an important one in the affairs of the Medical Society of Delaware. In the first place, it is a legislative year. The 80th Congress is now in session, and while the voice of the people last November unmistakably declared they wanted no further truck with the socialization of the American people, *including medicine,* and while the Wagners, Murrays, Dingles, Peppers, et al., are now hopping on the ground because their wings have been clipped, there will be proposed legislation looking to the improvement of medical service to those who can afford it least or not at all. The Taft bill (S. 140) was introduced in the Senate on January 10th, and the Miller bill (H. R. 605) on January 7th in the House, both aiming to establish a National Department of Health. Out of the hearings and the discussions anent the bills may come some constructive national legislation, but it behooves the profession to keep a weather eye on Congress just the same.

In the second place, the Delaware Legislature is also in session, and while our Society is sponsoring only the Premarital Bill, it will be wise to watch the grist from other sources that goes into the mill. Verbum sapiens sufficit.

In the third place, the City Council of Wilmington is still sitting, and the doctors of this city have not forgotten or forgiven that outrageous hike of June 27 in the annual city medical license fee from $10 to $50 per year (other cities take notice, but don't imitate—it may not be as healthy as it looks). At the hearing on September 26th the doctors were told to pay the new fee, and as, when, and if the fee was adjusted (to the $20 the doctors thought was fair), a refund would be made. Now the city clerk is mailing bills for $50 to those physicians who held out, in hope of a decent or at least some, reconsideration. Since it is thus belatedly evident that no consideration is planned at all, Wilmington physicians should pay this $50 license fee under protest, and then support the New Castle County Medical Society in its efforts to ameliorate their situation.

In the fourth place, the rewriting of the Constitution and By-Laws of the Society, authorized in 1941 and delayed only because of the war, must be done this spring. With the help of the Bureau of Legal Medicine of the A. M. A. the proper draft will be made, and a Constitutional Convention, the first since 1923, will be called to complete this important task.

In the fifth place, following the rewriting of the State Society's By-Laws, must come the long-postponed rewriting of the By-Laws of the New Castle County Medical Society, which is important to the State Society because this County Society comprises 77% of the members of the State Society.

In the sixth place, the A. M. A. celebrates its centennial anniversary at Atlantic City, June 9-13th. Delaware, as a near neighbor to the convention city, will be called upon to do more than its average at this outstanding celebration. Just what our Society may be asked to do or afford to do, is not known at this writing, but whatever the national organization asks us to do we shall try to do with credit to our Society, the second oldest state society in the Union. Appropriately, the convention is to be held in New Jersey, which has the oldest state society.

In the seventh place, we hope to have an outstanding session of our own Society in Wilmington in October. The last really great session was held in 1939, the Sesquicentennial Session. This year's session, celebrating the centennial of the national organization, should also be a memorable one in Delaware, and plans will be formulated to make it just that. We hope to renew the "Public Meeting" feature and to present there speakers from the national scene. The 1947 session, we hope, will be one of those you will remember.

In the eighth place, this year, above all recent years, is to be a year of closer cooperative effort. Just because the individual doctor, who has been your editor for the past thirty-one years (and who now has risen to third place, in years of service, as a state medical journal editor in the United States) is also your President for this one and only year, is no reason why any member should expect him and his aides to do it all. The *President* of the Society is not *the Society*—no individual member ever is.

And so, dear members, all of your officers bespeak your earnest assistance in making the year 1947 a memorable one in the annals of our beloved Society. In prospect the year means responsibility; in retrospect, let us make it mean accomplishment.

1789—MEDICAL SOCIETY OF DELAWARE—1947

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